

AMENDMENTS TO THE CLAIMS:

Please cancel claim 6, claims 14-46 and claim 48 without prejudice or disclaimer.

Please substitute currently amended claims 1-5, 7-13, 47, and 49-53 for the original claims having the same claim numbers.

Please add new claims 54-59 for consideration.

1. (currently amended) A method for disrupting survival signaling from the microenvironment ~~in~~ to cancer cells, ~~wherein said disrupting results in sensitizing cells to chemotherapy, biological therapies or radiation therapy of primary tumors, cancer metastases or micrometastases and hyperproliferative disorders in a mammal~~ said method comprising administering an agent effective in blocking the interaction of an integrin with an extracellular matrix protein of the microenvironment or that downregulates expression of said integrin.
2. (currently amended) The method of claim 1, wherein ~~said the method comprises blocking the interaction of integrins with the extracellular matrix proteins of the microenvironment~~ results in sensitizing cells to chemotherapy, biological therapies or radiation therapy of primary tumors, cancer metastases or micrometastases and hyperproliferative disorders in a mammal.
3. (currently amended) The method of claim 2 ~~1~~, wherein ~~said the integrins are~~ is selected from the group consisting of alpha 5 and/or beta 1 integrins and wherein said the extracellular matrix protein is fibronectin.
4. (currently amended) The method of claim 1, wherein ~~said the cancer cell is a breast cancer cell or a prostate cancer cell.~~
5. (currently amended) The method of claim 2 ~~1~~, wherein ~~said method comprises administration of the agent is selected from the group consisting of an antibody~~

specific for an integrin, ~~or a blocking peptide, or and a modified peptide that effective~~
to disrupts interaction of the integrin with the extracellular matrix.

6. (canceled)

7. (currently amended) A The method of claim 1, ~~said method comprising~~
~~administration of~~ wherein the agent is all trans retinoic acid or a retinoic acid
derivative.

8. (currently amended) The method of claim 1, wherein ~~said method comprises~~
~~decreasing expression of cell surface integrins with~~ the agent is a kinase inhibitor or a
transcription inhibitor.

9. (currently amended) The method of claim 1, wherein ~~said~~ the method comprises
blocking survival signaling initiated by ligation of integrins by microenvironment
proteins.

10. (currently amended) The method of claim 1, ~~said method comprising treatment~~
~~with~~ wherein the agent is an inhibitor of a kinase, said kinase selected from the group
consisting of MEP/MAP kinase, p38, RhoA, Rho kinase, PI3 kinase, PKC, and PKA.

11. (currently amended) The method of claim 10, wherein ~~said~~ the inhibitor is
selected from the group consisting of LY294002, UO 126, AG82, Y27632,
SB203580, PD169316, PD98059, RO318220, and a C3 transferase inhibitor.

12. (currently amended) A method of inhibiting cellular proliferation or inducing cell
death or cellular differentiation or for treating a cancer or a hyperproliferative
disorders in a mammal comprising ~~administration of~~ administering an agent capable
of downregulating expression of an integrin or blocking the binding of an integrins
with to the an extracellular matrix protein.

13. (currently amended) The method of claim 12, wherein ~~said~~ the integrins ~~comprise~~
is selected from the group consisting of alpha 5 and/or beta 1 and wherein ~~said~~ the
extracellular matrix protein is fibronectin.

14. (canceled)

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46. (canceled)

47. (currently amended) ~~A~~ The method of inhibiting cellular proliferation or inducing cell death or cellular differentiation in a mammal suffering from a disease or a disorder characterized by cellular proliferation claim 12, said method comprising administering a therapeutically effective amount of wherein the agent is a kinase inhibitor or a transcription inhibitor, and wherein the kinase inhibitor or transcription inhibitor is administered prior to, or concurrent with chemotherapy or radiation therapy.

48. (canceled)

49. (currently amended) The method of claim 48 12, wherein ~~said~~ the cancer is selected from the group consisting of breast cancer and prostate cancer.

50. (currently amended) The method of claim 47, wherein ~~said~~ the kinase inhibitor or transcription inhibitor downregulates expression of alpha 5 integrins or beta 1 integrins or phosphorylation of Akt ~~to sensitize for or potentiate chemotherapy or radiation therapy in mammals in need thereof~~.

51. (currently amended) The method of claim 47, wherein ~~said~~ the kinase or transcription inhibitor is selected from the group consisting of inhibitors of MEP/MAP kinase, p38, RhoA, Rho kinase, PI3 kinase, ~~and/or~~ PKC, and PKA.

52. (currently amended) The method of claim 51, wherein ~~said the~~ inhibitors are is selected from the group consisting of LY294002, UO 126, AG82, Y27632, SB203580, PD169316, PD98059, RO318220, and a 3 transferase inhibitor.

53. (currently amended) ~~A The method of treating cancer or a hyperproliferative disorder in a mammal claim 12, the method comprising administration of~~ administering an antibody effective to block integrin alpha 5 or beta 1 blocking antibodies or fibronectin-binding blocking peptides a peptide effective to block fibronectin or a modified peptides peptide effective to block fibronectin, or any combinations thereof, wherein the antibody or peptide is administered prior to or concurrent with a chemotherapeutic agent or radiation therapy.

54. (new) The method of claim 50, wherein the method results in sensitizing to, or potentiating chemotherapy or radiation therapy in mammals undergoing treatment for a cancer or a hyperproliferative disorder.

55. (new) A pharmaceutical composition comprising an agent capable of downregulating expression of alpha 5 and/or beta 1 integrins or capable of inhibiting the binding of the integrins to the extracellular matrix, and a pharmaceutically acceptable carrier.

56. (new) The composition of claim 55, wherein the agent is selected from the group consisting of a kinase inhibitor and a transcription inhibitor.

57. (new) The composition of claim 56, wherein the kinase or transcription inhibitor is selected from the group consisting of inhibitors of MEP/MAP kinase, p38, RhoA, Rho kinase, PI3 kinase, PKC, and PKA.

58. (new) The composition of claim 57, wherein the inhibitor is selected from the group consisting of LY294002, UO 126, AG82, Y27632, SB203580, PD169316, PD98059, RO318220, and a 3 transferase inhibitor.

59. (new) The composition of claim 55, wherein the agent is selected from the group consisting of an antibody effective to block integrin alpha 5 or beta 1, a peptide effective to block fibronectin, a modified peptide effective to block fibronectin, and any combinations thereof, wherein the antibody or peptide is administered prior to or concurrent with a chemotherapeutic agent or radiation therapy.